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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,935	08/02/2001	Brigitte Bathe	211712US0X	5782
22850	7590	10/12/2005	EXAMINER	
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			HUTSON, RICHARD G	
			ART UNIT	PAPER NUMBER

1652

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/919,935

Applicant(s)

BATHE ET AL.

Examiner

Richard G. Hutson

Art Unit

1652

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 August 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 23 September 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

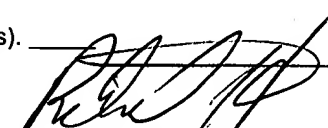
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: 56-58.
Claim(s) objected to: 37-39, 45, 49, 80.
Claim(s) rejected: 34, 36, 40-44, 46-48, 50-55, 59-79 and 81.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.


Richard G. Hutson, Ph.D.
Primary Examiner
Art Unit: 1652

Continuation of 5. Applicant's reply has overcome the following rejection(s): Applicants amendment has overcome the new matter rejection under 35 USC 112 1st paragraph.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 34, 36, 40-44, 46-48, 50-55, 59-79 and 81 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2, wherein said protein has methylene tetrahydrofolate reductase activity, does not reasonably provide enablement for any polynucleotide which encodes a polypeptide which is merely 90% identical to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 34, 36, 40-44, 46-48, 50-55, 59-79 and 81. In response to this rejection applicants have amended claims 34, 36, 38, 39, 54, 59, 70, 72 and 73 and traverse the rejection as it applies to the newly amended claims.

Applicants have amended the claims such that they no longer refer to those polypeptides having 90% identity to fragments of SEQ ID NO: 2. Otherwise, the scope of the claims remains unchanged in that the claims are directed to any polynucleotide which encodes a polypeptide which is merely 90% identical to SEQ ID NO: 2, wherein said polypeptide has methylene tetrahydrofolate reductase activity. Applicants submit that the rejection is moot because based on the state of the art in molecular biology as well as guidance provided by the specification it would require undue experimentation to make and use a polynucleotide that encodes a polypeptide having at least 90% identity to SEQ ID NO: 2 wherein said polypeptide has methylene tetrahydrofolate reductase activity. Applicants submit that once a coding sequence is known, it is routine to make fragments and assay such fragments for enzymatic activity such as tetrahydrofolate reductase activity.

Applicants complete argument is acknowledged, however, not found persuasive for the reasons previously stated and repeated below. First, it is noted that contrary to applicants argued genus, the subject matter that is rejected is not "fragments of SEQ ID NO: 2 having tetrahydrofolate reductase activity", but rather those variants of SEQ ID NO: 2 that have a mere 90% sequence identity to SEQ ID NO: 2 having tetrahydrofolate reductase activity.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a methylene tetrahydrofolate reductase) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without the desired activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus applicants have not provided sufficient guidance as to how to make the majority of those polynucleotides of the claimed genus encoding such polypeptides (i.e. that genus of polynucleotides encoding such polypeptides and having 90% identity to a fragment of SEQ ID NO:2).

Claims 37-39, 45, 49, 54 and 80 remain objected to because of the following informalities: Claims 37-38, 45, 49 and 80 are dependent on rejected claim 34..